

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Cancer in deceased adults with intellectual disabilities: English population-based study using linked data from three sources
<b>AUTHORS</b>	Heslop, Pauline; Cook, Adam; Sullivan, Brian; Calkin, Rachel; Pollard, Johanna; Byrne, Victoria

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Landes, Scott Syracuse University, Department of Sociology and Aging Studies Institute
<b>REVIEW RETURNED</b>	14-Oct-2021

<b>GENERAL COMMENTS</b>	<p>First and foremost, there is a dire need for this study as the topic of cancer in people with intellectual disability is sorely under-researched. Thank you to the authors for their work on this topic. The study is quite informative and will provide a substantial contribution to the field that can have immediate impacts on medical practice and public health efforts to reduce premature mortality among a vulnerable health population.</p> <p>I have one major concern and a few minor concerns. My major concern is with the presentation of the results. As I read the study, you essentially have four interrelated, but distinct samples: adults identified by LeDeR with cancer (N=1096); adults with linkage to the cancer registry (N=771); adults with information on route to diagnosis (N=462); and adults with death certificate data (N=852). As presented, the results address specific outcomes for the latter 3 samples, but do so in a manner that I think could lead to some confusion on the part of readers. I found myself going back and forth between the results section to clarify which group I was reading about. My suggestion would be to provide a clear definition and distinction for each of these four interrelated groups in the analytic section with a thorough description of the strategy of how results will be presented. I also suggested placing signposts at the beginning of each section to indicate the shifts between these samples. I found each separate section of the results quite compelling – just had to engage in a bit of extra work to clarify my place in each section that I am concerned could discourage some readers. I also would like to see a more comparative Table 1 that includes as much demographic information as possible for each of these samples. This would help give a better idea of the ways in which the results for each section with lesser cases may be biased – a topic that will need to be addressed in the limitation section. I feel the focus and emphases of the paper are on target, but think these suggested edits will provide a more focused and clearer presentation of these important findings.</p>
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	<p>Minor suggestions:</p> <p>Reference NHS for the stages definitions (appears to be from their website). Specify reason for not including Stage 0?</p> <p>Were UCODs corrected for inaccurate reporting of ID?</p> <p>Is it possible to provide a comparison of the potentially avoidable deaths among those with ID to data from the general population?</p>
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<b>REVIEWER</b>	Mahar, Alyson University of Manitoba College of Medicine, Community Health Sciences
<b>REVIEW RETURNED</b>	12-Nov-2021

<b>GENERAL COMMENTS</b>	<p>The authors perform a linkage between a registry of people who died with intellectual disabilities and the national cancer registry in England. The authors set out to describe the types of cancers diagnosed in people with ID, their stage at diagnosis, and their cause of death. Unfortunately the research questions do not align with the available data. Only those people with cancer who died were eligible for inclusion in the study. Many others may be alive with cancer, and these people were not included. This selection bias would affect what cancers are reported, the stage at which they were diagnosed, and their cause of death. The methods employed in the study and statistical comparisons presented in the results do not map onto the research questions and there are not enough (or any) details provided in the methods section. For example, although statistical comparisons are made with a general cancer population, this was not referenced in the research questions and this cancer population is not mentioned or described in the methods section. Are these all living people with cancer? Or also decedents?</p> <p>There are very little data on cancer among people with ID and this rich linkage has the potential to provide a description of cancer diagnoses among people who died with ID. This study would be better framed as a short, detailed, descriptive report on people with ID and cancer, who died. Alternatively, if the goals are to compare the risk and stage of diagnosis of cancer for people with ID to the general population, different study populations and data sources should be identified.</p>
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## VERSION 1 – AUTHOR RESPONSE

Reviewer 1: Prof. Scott Landes, Syracuse University	
<p>I have one major concern and a few minor concerns.</p> <p>My major concern is with the presentation of the results. As I read the study, you essentially have four interrelated, but distinct samples: adults identified by LeDeR with cancer (N=1096); adults with linkage to the cancer registry (N=771); adults with information on route to diagnosis (N=462);</p>	<p>Thank you for this suggestion which we have taken up. We think that this does make the baseline numbers clearer.</p> <p>We have introduced three groupings at the end of the 'Analysis' section, and regularly reminded the reader about which grouping is under consideration in the Findings section.</p> <p>The grouping we have used are as follows:</p>

<p>and adults with death certificate data (N=852). As presented, the results address specific outcomes for the latter 3 samples, but do so in a manner that I think could lead to some confusion on the part of readers. I found myself going back and forth between the results section to clarify which group I was reading about. My suggestion would be to provide a clear definition and distinction for each of these our interrelated groups in the analytic section with a thorough description of the strategy of how results will be presented. I also suggested placing signposts at the beginning of each section to indicate the shifts between these samples. I found each separate section of the results quite compelling – just had to engage in a bit of extra work to clarify my place in each section that I am concerned could discourage some readers.</p>	<p>Group 1: Adults with intellectual disabilities known from LeDeR data to have died with cancer (n=1,096).</p> <p>Group 2: Adults with intellectual disabilities known from LeDeR data to have died with cancer and for whom linked data were available from the national cancer registry (n=771).</p> <p>Group 3: Adults with intellectual disabilities known from LeDeR data to have died with cancer and for whom official cause of death coding from NHS Digital indicated cancer as their underlying cause of death (n=852).</p>
<p>I also would like to see a more comparative Table 1 that includes as much demographic information as possible for each of these samples. This would help give a better idea of the ways in which the results for each section with lesser cases may be biased – a topic that will need to be addressed in the limitation section.</p> <p>I feel the focus and emphases of the paper are on target, but think these suggested edits will provide a more focused and clearer presentation of these important findings.</p>	<p>We have amended Table 1 to include demographic information about adults with intellectual disabilities in each of the three groupings described above.</p> <p>We have removed the male/female breakdown in this Table, as this was not relevant to the text and allows a less cluttered table that is easier to read.</p>
<p>Minor suggestions:</p>	
<p>Reference NHS for the stages definitions (appears to be from their website). Specify reason for not including Stage 0?</p>	<p>The cancer staging system is taken from Cancer Research UK (see: <a href="https://www.cancerresearchuk.org/about-cancer/what-is-cancer/stages-of-cancer#types">https://www.cancerresearchuk.org/about-cancer/what-is-cancer/stages-of-cancer#types</a>).</p> <p>Stage 0 refers to 'carcinoma in situ', 'precancerous changes' or 'non invasive cancer' and many of these will never develop into cancer. For this reason we have not included them in this study. We have added a reference for the source information in the main text.</p>
<p>Were UCODs corrected for inaccurate reporting of ID?</p>	<p>These have not been corrected and we have confirmed this in the main text.</p>

<p>Is it possible to provide a comparison of the potentially avoidable deaths among those with ID to data from the general population?</p>	<p>A breakdown of types of neoplasms that are preventable or treatable is not reported for the general population by the UK Office for National Statistics.</p>
<p>Reviewer: 2 Dr. Alyson Mahar, University of Manitoba College of Medicine</p>	
<p>The authors perform a linkage between a registry of people who died with intellectual disabilities and the national cancer registry in England. The authors set out to describe the types of cancers diagnosed in people with ID, their stage at diagnosis, and their cause of death. Unfortunately the research questions do not align with the available data. Only those people with cancer who died were eligible for inclusion in the study. Many others may be alive with cancer, and these people were not included. This selection bias would affect what cancers are reported, the stage at which they were diagnosed, and their cause of death.</p> <p>The methods employed in the study and statistical comparisons presented in the results do not map onto the research questions and there are not enough (or any) details provided in the methods section. For example, although statistical comparisons are made with a general cancer population, this was not referenced in the research questions and this cancer population is not mentioned or described in the methods section. Are these all living people with cancer? Or also decedents?</p>	<p>Thank you for this comment. It has been helpful to reflect on what we can and cannot compare our data to.</p> <p>We have amended the research question to better reflect the analyses reported in this paper. The research questions now read:</p> <ol style="list-style-type: none"> <li>1.What are the types of cancer diagnosed in adults with intellectual disabilities who have died?</li> <li>2.How, and at what stage, was cancer diagnosed in adults with intellectual disabilities who have died?</li> <li>3.What is the underlying cause of death in adults with intellectual disabilities known to have had cancer?</li> </ol> <p>We have added a section to the Methods section to describe the general population data that we have used for comparative purposes. This confirms that they are also decedents.</p> <p>We have removed the general population data relating to stage and grade at diagnosis as these were not focused on decedents.</p>
<p>There are very little data on cancer among people with ID and this rich linkage has the potential to provide a description of cancer diagnoses among people who died with ID. This study would be better framed as a short, detailed, descriptive report on people with ID and cancer, who died. Alternatively, if the goals are to compare the risk and stage of diagnosis of cancer for people with ID to the general population, different study populations and data sources should be identified.</p>	<p>As we mentioned above, we have removed the general population data that does not relate to decedents. The remaining general population data, about underlying cause of death, has been retained.</p>

## VERSION 2 – REVIEW

<b>REVIEWER</b>	Landes, Scott Syracuse University, Department of Sociology and Aging Studies Institute
<b>REVIEW RETURNED</b>	12-Jan-2022

<b>GENERAL COMMENTS</b>	<p>My concerns from the prior review were addressed. Only minor suggestions at this point. Look forward to seeing this study in print. Great work.</p> <p>The points made on page 6, lines 16-17 is directly supported with empirical evidence showing rates of inaccurate reporting of ID on death certificated in the US is much less likely when a cancer dx is present at the time of death: Landes, Scott D., Margaret A. Turk and Erin Bisesti. 2021. "Uncertainty and the Reporting of Intellectual Disability on Death Certificates: A Cross-Sectional Study of US Mortality Data from 2005 to 2017." <i>BMJ Open</i> 11(1):e045360. doi: 10.1136/bmjopen-2020-045360.</p> <p>Unless I am misreading the statement, the percentage reported on page 10 lines 25-26 should be 21%.</p> <p>For consistency, I suggest reporting the percentage on page 10, line 20 as well – 9%.</p> <p>On page 12, line 44-45, I would also highlight that 66% of cancers were dx at Stage 3 or above as much of the literature on late stage dx discusses stage 3 and above. I am not sure the trustworthiness of the source, but Cancer Research UK reports 46% of general pop in England has late state dx, making this finding of 66% quite remarkable. If you deem this, or any other data of distribution of stage dx in the UK reliable, I think it would be beneficial to include comparison in the paper.</p> <p>Make the parenthetical statement on page 13, lines 27-30 a separate sentence.</p>
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## VERSION 2 – AUTHOR RESPONSE

Thank you for the care that the reviewers have taken in checking this paper. In response to the further amendments, our response is as follows:

Reviewer: The points made on page 6, lines 16-17 is directly supported with empirical evidence showing rates of inaccurate reporting of ID on death certificated in the US is much less likely when a cancer dx is present at the time of death.

Response: Thank you for this comment and the reference supplied. We have added this information into the Discussion where we feel it is best positioned.

Reviewer: Unless I am misreading the statement, the percentage reported on page 10 lines 25-26 should be 21%.

For consistency, I suggest reporting the percentage on page 10, line 20 as well – 9%.

Response: We have checked the percentages, and added the percentages where we feel it would

add clarity, as indicated.

Reviewer: On page 12, line 44-45, I would also highlight that 66% of cancers were dx at Stage 3 or above as much of the literature on late stage dx discusses stage 3 and above.

Response: We have added this.

Reviewer: Make the parenthetical statement on page 13, lines 27-30 a separate sentence.

Response: We have removed the brackets from this statement.

09/02/2022 - re the Reference citation missing. We have corrected this and checked the remainder of the references.